

WE CLAIM:

- 1 1. An electrode comprising:
- 2 a non-corroding, conducting wire coated with
- 3 an insulating polymer;
- 4 a recess at one end of said coated wire,
- 5 forming a channel in the insulating polymer coat devoid
- 6 of wire and bounded at one end by the wire and at an
- 7 opposite end by the environment adjacent the coated
- 8 wire;
- 9 a multilayered polymeric composition within
- 10 said channel, the composition comprising:
- 11 a redox layer adjacent to and contacting
- 12 said wire, the redox layer comprising a redox enzyme
- 13 crosslinked to a redox polymer;
- 14 a biocompatible polymer layer adjacent to the
- 15 environment outside the coated wire; and
- 16 an analyte diffusion limiting barrier layer
- 17 positioned between said redox layer and said
- 18 biocompatible layer.

- 1 ~~2. A method for producing an in vivo glucose~~
- 2 ~~biosensor comprising the steps of:~~
- 3 ~~coating a non-corroding metal or carbon wire~~
- 4 ~~with a biocompatible insulating polymer containing less~~
- 5 ~~than 5% water when in equilibrium with physiological~~
- 6 ~~body fluids to form a coated wire;~~
- 7 ~~etching said coated wire to form a recess at~~
- 8 ~~one end of said coated wire, said recess devoid of~~
- 9 ~~metal or carbon;~~
- 10 ~~immobilizing within said recess, adjacent to~~
- 11 ~~said wire, a redox composition comprising glucose~~
- 12 ~~oxidase and a redox polymer;~~

13 ~~overcoating contents of the recess with a~~
 14 ~~biocompatible polymer;~~
 15 ~~wherein said etched wire with said polymer~~
 16 ~~overcoated recess and contents form a glucose biosensor~~
 17 ~~having substantially no current output at zero glucose~~
 18 ~~concentration, even in the presence of interfering~~
 19 ~~electroreactive species.~~

1 3. A method for measuring glucose
 2 concentration in an animal comprising the steps of:
 3 implanting subcutaneously in an animal the
 4 electrode of claim 1;
 5 placing a second reference counter or
 6 combined reference and counter electrode on or in the
 7 skin of the animal;
 8 connecting the electrodes through an
 9 electrical circuit; and
 10 obtaining readings to measure glucose
 11 concentration.

1 4. The method of claim 3, wherein at least
 2 two electrodes of claim 1 are implanted subcutaneously
 3 in said animal, and wherein paired readings of said two
 4 electrodes that do not differ more than two standard
 5 deviations are accepted as correctly measuring the
 6 concentration of glucose.

1 5. A biosensor comprising:
 2 a non-corroding metal or carbon electrode;
 3 a sensing layer adjacent to and in electrical
 4 contact with the electrode, the sensing layer
 5 ~~comprising a redox polymer and a redox enzyme;~~

6 ~~a biocompatible layer coating an outer~~
 7 ~~surface of the electrode and sensing layer and adjacent~~
 8 ~~to an environment outside the sensor, said~~
 9 ~~biocompatible layer comprised of a biocompatible~~
 10 ~~polymer containing not less than 20% water by weight~~
 11 ~~when in equilibrium with physiological body fluids.~~

1 6. The biosensor of claim 5, wherein said
 2 electrode is part of an electrically conducting wire.

1 7. The biosensor of claim 1, wherein said wire is
 2 coated along its length, but not at its tip, with an
 3 electrically insulating polymer containing less than 5%
 4 water by weight when in equilibrium with physiological
 5 body fluids.

1 8. The biosensor of claim 7, wherein said tip of
 2 the wire is recessed in the insulating polymer coat,
 3 forming a recessed channel having a length from tip of
 4 the sensor to the recessed wire of between
 5 approximately 20 μm and 1 mm.

1 9. The biosensor of claim 8, wherein said redox
 2 polymer is derived from poly(1-vinylimidazole) or a
 3 copolymer of (1-vinyl imidazole) bound to a metal ion
 4 selected from the group consisting of $\text{Os}^{3+/2+}$, $\text{Ru}^{3+/2+}$, and
 5 $\text{Fe}^{3+/2+}$.

1 10. The biosensor of claim 1, wherein the redox
 2 potential of said redox polymer is not more reducing
 3 than about -0.15V and not more oxidizing than about
 4 +0.15V versus the standard calomel electrode in an
 5 ~~aqueous solution at about pH 7.4.~~

1 ~~11. The biosensor of claim 1 further comprising~~
2 ~~an interference eliminating layer comprising a~~
3 ~~peroxidase enzyme.~~

1 12. The biosensor of claim 1, wherein said redox
2 enzyme catalyzes the oxidation of glucose.

1 13. The biosensor of claim 12, wherein said redox
2 enzyme is glucose oxidase.

1 14. The biosensor of claim 13, wherein said redox
2 enzyme is recombinant glucose oxidase.

1 15. The biosensor of claim 1, wherein said redox
2 enzyme catalyzes the oxidation of lactate.

1 16. The biosensor of claim 11, wherein said
2 interference eliminating layer further comprises an
3 enzyme which catalyzes a hydrogen peroxide-generating
4 reaction.

1 17. The biosensor of claim 7, wherein said
2 insulating polymer is selected from the group
3 consisting of polyimide, polyester, polyurethane, and
4 perfluorinated polymer.

1 18. The biosensor of claim 1, further comprising
2 a glucose flux limiting layer positioned between said
3 sensing layer and said biocompatible layer, the glucose
4 flux limiting layer comprising a polyanionic,
5 polycationic, or zwitterionic polymer.

1 ~~19. The biosensor of claim 1 wherein the outside~~
2 diameter of the insulated wire is less than about
3 0.3mm.

1 20. The biosensor of claim 1 wherein the redox
2 enzyme and redox polymer are crosslinked.

1 21. A method for manufacturing the biosensor of
2 claim 6, comprising the steps of:
3 electrically charging droplets of an aqueous
4 polymer;
5 applying a potential to the electrode such that
6 the electrically charged droplets are attracted to said
7 electrode; and
8 applying the charged droplets of polymer to the
9 electrode to form a polymer coated electrode.

1 22. The method of claim 21, wherein the
2 electrically charged droplets are applied to a non-
3 insulated tip of an electrically insulated wire.

1 23. A method for manufacturing the biosensor of
2 claim 1, wherein said recessed channel is formed by
3 electrolytic dissolution of part of the electrically
4 conducting wire, with an oxidizing electrical potential
5 of not less than 0.3 volts versus the standard calomel
6 electrode being maintained on the dissolving wire, said
7 wire being immersed in an aqueous solution containing
8 at least one anion selected from the group consisting
9 of CN^- , Cl^- , Br^- , and I^- at a concentration of at least
10 approximately 0.1M.

1 24. A method for measuring the concentration of a
2 ~~biochemical in an animal comprising:~~

3 ~~contacting body fluid of an animal the electrode~~
4 of claim 1; and

5 determining from the electrical signal generated
6 at the electrode the concentration of biochemical in
7 the body fluid.

1 25. The method of claim 25, wherein said
2 contacting is implanting the electrode subcutaneously.

1 26. The method of claim 25, wherein said
2 subcutaneous tissue is blood.

1 27. The method of claim 24, wherein said
2 biochemical is glucose.

1 28. The method of claim 24, wherein said
2 biochemical is lactate.

1 29. The method of claim 24, wherein at least two
2 electrodes are simultaneously implanted and wherein
3 their readings are compared and accepted as valid only
4 when they do not differ by more than two standard
5 deviations, the standard deviations being calculated
6 from paired measurements with a pair of implanted
7 electrodes.

1 30. A method for calibrating the implanted
2 electrode of claim 1, comprising the steps of:
3 analyzing the concentration of the analyte to be
4 measured by the electrode of claim 8 in one or more
5 samples of fluid withdrawn from a patient, where the
6 concentration of the chemical does not change
7 ~~substantially in the withdrawn samples;~~

8 ~~relating the current generated by the electrode at~~
9 ~~the time the sample is withdrawn to the concentration~~
10 ~~of biochemicals.~~

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